

methods of screening for calpain modulators. The Office Action requires the Applicants to elect one of the calpain 10 polypeptide sequences designated a-h as the invention to be examined.

As the specification makes clear, the different SEQ ID NOs for calpain 10 represent polypeptides that result from alternative splicing of the same gene based on individual samples. Specification at page 139, lines 5-10. The restriction is inappropriate because the sequences have considerable overlap and identity with one another, and thus their chemical structures are similar. Imposition of a species election, in contrast to a restriction, is more appropriate.

Furthermore, U.S. Patent No. 6,235,481 has claims directed to the different species of calpain 10 polypeptides. Claim 1 recites:

An isolated and purified polynucleotide comprising a region encoding human *calpain* 10a, human *calpain* 10b, human *calpain* 10c, human *calpain* 10d, human *calpain* 10e, human *calpain* 10f, human *calpain* 10g, human *calpain* 10h, or mouse *calpain* 10.

Claim 57 of the patent recites:

A method of obtaining a human *calpain* 10a, human *calpain* 10b, human *calpain* 10c, human *calpain* 10d, human *calpain* 10e, human *calpain* 10f, human *calpain* 10g, human *calpain* 10h, or mouse *calpain* 10 polypeptide comprising:

a) obtaining a polynucleotide comprising a region encoding a human *calpain* 10a, human *calpain* 10b, human *calpain* 10c, human *calpain* 10d, human *calpain* 10e, human *calpain* 10f, human *calpain* 10g, human *calpain* 10h, or mouse *calpain* 10;

b) inserting the polynucleotide into a host cell; and

c) culturing the host cell under conditions sufficient to allow production of the human *calpain* 10a, human *calpain* 10b, human *calpain* 10c, human *calpain* 10d, human *calpain* 10e, human *calpain* 10f, human *calpain* 10g, human *calpain* 10h, or mouse *calpain* 10 polypeptide; wherein a human *calpain* 10a, human *calpain* 10b, human *calpain* 10c, human *calpain* 10d, human *calpain* 10e, human *calpain* 10f, human *calpain* 10g, human *calpain* 10h, or mouse *calpain* 10 polypeptide is thereby obtained.

Thus, these nucleic acid and amino acid sequences are novel and nonobvious. The present claims under restriction are directed to methods of screening involving calpain 10a, b, c, d, e, f,

g, and h. An extensive search for the calpain 10 species would not be undue on the examiner because the sequences are novel and have already been determined by the PTO as such.

Applicants also contend that restricting the present screening method claims to at least 10 different inventions (in this *second* Restriction Requirement) based on alternative splicing of the same gene is costly and unfair to the Applicants and their assignee, the University of Chicago.

Nonetheless, as is required, Applicants elect, with traverse, to prosecute calpain a, which has the amino acid sequence of SEQ ID NO:2. Moreover, because claims 18, 19, 52, and 53 are proper linking claims, should they be allowed, claim 54 should be examined under MPEP § 809 as to nonelected inventions.

The Examiner is invited to contact the undersigned attorney at (512) 536-3081 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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